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Bioreactor Engineering Research and Industrial Applications II

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Preface

Bioreactor is the core of industrial biotechnology practice. Traditional bioreactors include enzyme reactors and microbial fermentors, but recent research activities on bioreactors have significantly extended to various scales of them whether in a large natural ecology system or at a micro-scale level of nano sizes. Although bioreactor and bioreactor technology seem to be a traditional area of biochemical engineering and biotechnology, recently some new types of bioreactors have still been developed and applied into industrial practice. New methodology concepts on bioreactor research have also been proposed on the basis of cell biology and metabolic engineering. Therefore, in this context, this special volume is dedicated to bioreactor engineering to make the old new, and six invited chapters ranging from novel design of bioreactors to methodologies of bioreactor/bioprocess analysis and optimization are included.

As well known, gas-liquid contacting is an important unit operation in chemical and biochemical processes, and the gas utilization efficiency is generally low in conventional gas-liquid contactors, especially for sparingly soluble gases such as O₂, carbon monoxide (CO) and hydrogen (H₂). Ye et al. [1] described a novel self-inducing reactor for gas phase substrate utilization to break the barrier on gas-liquid transfer. The gas self-inducing impeller is able to recycle gas in the headspace of a reactor to the liquid bulk without utilization of additional equipment like a gas compressor, and its gas utilization efficiency is significantly enhanced. The authors introduced the principle, design, characteristics of self-inducing reactors as well as their application to biotechnology. Such as bioreactor may find its significant impact in CO and H₂ utilization by biotechnological approach.

H₂ is currently an important commodity chemical with its global annual market of about 45 million tons per year and a steady increase in demand over the last decades. It has the potential to become the future dominant transportation fuel. Technologies such as in vitro synthetic pathway biotransformation, by using over 10 enzymes to catalyze unnatural catabolic pathways, enable the H₂ storage in the form of carbohydrates [2]. Therefore, in vitro H₂ generation represents a clear opportunity for novel bioreactor and system design. This system is demonstrated

with the conversion of glucose to H_2 at a high rate and the H_2 production from glucose 6-phosphate at a greatly increased reaction rate [2].

Healthcare and biomedical engineering is another important area of applied biotechnology. Traditional cultivation engineering of animal cells was developed from 1980s to industrialize the production of animal cell products such as interferon, interleukins, cytokines, tissue plasminogen activator, and therapeutic antibodies. The widespread use and industrialization of regenerative medicine are being highly expected because of the recent rapid progress in basic life sciences concerning human stem cells. Because the control of proliferation and differentiation of human cells and their three-dimensional culture into tissue are necessary for the realization of regenerative medicine in which cells are the final product, some new technologies of cell processing engineering, different from the conventional animal cell cultivation technology, should be developed. The cell quality such as cell heterogeneity should be noninvasively estimated before transplantation to patients, because cultured cells are usually heterogeneous and most protocols of regenerative medicine are autologous system. Takagi [3] reviewed the cell processing engineering including automatic cell processing and noninvasive cell quality estimation of adherent mammalian cells for regenerative medicine.

Lignocellulosic biomass utilization and biorefinery is another hot topic in recent years around the world, while pretreatment is a crucial step for overcoming the recalcitrance of lignocellulosic biomass in biorefinery processing. Pretreatment also affects both upstream and downstream operations beyond itself, and the efficiency of a biorefinery process is highly dependent on pretreatment technology used, such as pretreatment method, severity, inhibitors generated, wastewater discharge, residues released, and the reactors used. High solid loading in biomass pretreatment becomes a reasonable option and trend in the future industrial pretreatment operation. Zhang et al. [4] summarized the types, geometry, and design principle of pretreatment reactors at high solid loading of lignocellulose, which provided useful information for choosing and designing reactors of high-solids-loading biomass pretreatment.

In the last decades, targeted metabolic engineering of microbial cells has become one of the major tools in bioprocess design and optimization, for which detailed knowledge about relevant metabolic pathways and their regulation is required. Since *in vitro* experiments cannot display bioprocess conditions and behaviors properly, process-data about the cellular metabolic state has to be collected *in vivo*. Weiner et al. [5] highlighted several possibilities to gain information about the metabolic state of microorganisms, and summarized various methods to conduct perturbation experiments, which usually are the basis for detailed metabolic analyses and can be divided into dynamic and steady-state experiments.

In recent years, more and more efforts have been made for improving yields, titers, and productivities of aimed products through bioprocess engineering strategies. Among them, optimization and scale-up method for industrial processes are of great importance. It is indeed a permanent task and challenge for biochemical engineers to discover and gain more knowledge of cell kinetics and bioreactor fluid dynamics, and of the interaction between these two parts, in order to accelerate the

technology transition from laboratory study to real industrial application. Xia et al. [6] highlighted the methodology for process optimization and bioreactor scale-up by integrating fluid dynamics with kinetics. A comprehensive discussion on advantages and challenges of the model-driven scale-up method was also given.

Finally, we hope this book is providing some new fundamental knowledge as well as practical experience to colleagues in the field of biochemical engineering and industrial biotechnology, which will be helpful to the technology advancement. Here, we would like to thank all the contributing authors for their excellent collaboration, and our special appreciation goes to the Managing Editor Prof. Dr. Thomas Scheper, all the referees, and the publisher and the book-series editorial staffs at Springer for their constructive suggestions, continuous support and kind help during the entire process from this special volume preparation to its final publication.

Shanghai
October 2015

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